Remarks and Arguments

Claims 21-28 are pending in this case. Claims 22 and 23 have been withdrawn because the Office believes they are drawn to non-elected subject matter.

35 U.S.C. § 112

1. Enablement

Claims 21 and 24-28 stand rejected under 35 U.S.C. § 112 as allegedly not enabled. The Office admits that the specification discloses high levels of expression of PODXL in undifferentiated hES cells and decreased levels of PODXL expression after growing the hES cells in unconditioned culture media, where PODXL expression level is measured by real time PCR. The Office alleges that the specification fails to provide adequate guidance for how to measure the presence of undifferentiated hES cells by measuring PODXL protein expression level. According to the Office it was known in the art that cDNA or mRNA levels do not necessarily correspond to protein level expression. Applicants traverse the rejection.

a. The Legal Standard

As long as the specification discloses at least one method of making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. §112 is satisfied. *In re Fisher* 166 USPQ 18, 24 (CCPA 1970); *John Hopkins University v. Cellpro Inc.* 152 F3d 1342, 1361 (Fed Cir. 1998); *Amgen Inc. v. Hoechst Marion Roussel Inc.* 314 F.3d 1313, 1335 (Fed. Cir. 2003). A disclosure enables a claim if it contains sufficient information such that a skilled artisan in the pertinent art can make and use the claimed invention without undue experimentation. *In re Wands* 8 USPQ 2d 1400 (Fed. Cir. 1988). The burden rests with the USPTO in establishing that the claims are not enabled. MPEP §2164.04.

> It is incumbent upon the Patent Office, whenever a rejection on this basis [enablement] is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure **and to back up its assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement.** *In re Marzocchi* 169 U.S.P.Q. 367, 369 (CCPA 1971)(emphasis added).

The Office has not met its burden in this case.

b. Claims 21 and 24-28 Are Enabled

The Office presented several arguments in the Office Action dated May 21, 2008 as to why it believed the claims were not enabled. Applicants address each argument in turn.

Applicants note that the Economou reference submitted previously demonstrates that human PODXL mRNA levels correlate with protein expression levels. Nonetheless, the Office argues that the Economou reference discusses adult somatic cells not hES cells and "different types of cells and differentiation states **could** have diverse correlation between mRNA and protein expression levels" (emphasis added). "The correlation of mRNA and protein expression levels in human glomerula epithelial cells can not be extrapolated into the correlation between mRNA and protein expression level in human embryonic stem cells," (Office Action dated 5/21/08 page 3). Nothing in the record supports this position. The Office is reminded that it bears the burden of establishing non-enablement. Applicants have made of record a reference which contradicts the premise of the Office's position. The burden is now on the Office to "**back up its assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement.**" *In re Marzocchi*, supra. The Office has neither presented evidence nor reasoning that supports its position. Simply stated the Office has not produced a reference establishing a difference between protein and mRNA levels in human somatic cells versus stem cells. Nor has the Office explained with sound scientific reasoning why the alleged difference between somatic cells and stem cells exists. The Office has merely speculated ("could"). Speculation is not enough.

Applicants previously noted that the Office has only cited one reference, Spence, to support its position. Spence puts forth the general proposition that in yeast total mRNA does not correlate with protein expression. From this the Office extrapolates and states: "The cited reference Spence provides evidence that such notion is true in general. It is true in yeast gene expression and it is also true in mammalian gene expression," (Office Action dated 5/21/08, page 3). Applicants again remind the Office

of its burden. The Office has not provided any evidence or reasoning to support its position that expression levels of mRNA and protein do not correlate in mammals, based on the yeast data presented in Spence. The Office must either cite a reference establishing the alleged difference in mammalian cells or alternatively provide sound scientific reasoning to support its allegation that the yeast data may be extrapolated to mammals. In contrast, Applicants have cited two references that confirm Applicants position, i.e. PODXL mRNA and protein levels correlate in mammals.

Next the Office turns to the Hara reference which Applicants submitted to show that the expression of mRNA and protein for the murine homolog of PODXL correlate. In response the Office states:" Hara reference discloses that PCLP1 mRNA is detected in kidney, heart, lung, brain, and muscle, but not in spleen, thymus, small intestine, or liver of adult mice. Hara shows PCLP1 protein expression in aorta-gonad-mesonephros (AGM) endothelial line cells by immuno-staining with anti-PCLP1 antibody.... Expression of PCLP1 mRNA in kidney, heart, lung, brain, and muscle of adult mice does not correlate to expression of PCLP1 protein in AGM endothelial-like cells, which are precursors of hematopoietic stem cells," (Office Action dated 5/21/08, pages 3-4). Applicants note that the Hera states that mRNA analysis of the spleen and thymus indicated that PCLP1 was not expressed in the adult mouse (page 569, 1st paragraph), thus confirming again a correlation between RNA expression and protein expression for murine PCLP1.

Finally the Office alleges that tissue organ cultures comprise not only human ES cells but also various other cells that interact with the human ES cells and such interaction could change the gene and protein expression of the human ES cell in the organ culture. Applicants note, however, that the Office has failed to provide evidence or scientific reasoning to support its position and thus has not maintained its burden. The Office has failed to cite a single reference with regard to organ cultures. Moreover, Applicants believe the Office's assumptions are incorrect. Organ cultures are typically established from post implantation embryos and thus could not possibly contain hES cells (see, e.g., Okano et al. (2005) *Int. J. Dev. Biol.* 49:23). In this regard Applicants urge the Office to consider the description of hES cells in the specification which indicates that hES cells are obtained from pre-implantation, not post implantation

embryos (see page 7, lines 1-15). By the time the embryo implants all hES cells will have differentiated into another phenotype. Moreover, as previously argued to the extent that a culture does contain hES the method recited in the claims will work and the Office has not produced a single reference to suggest otherwise.

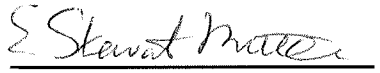
For all of the reasons set forth above, Applicants believe the claims are enabled. Withdrawal of the rejection is requested.

CONCLUSION

In view of the foregoing remarks, Applicants respectfully request the reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this filing and charge any additional required fees to our deposit account No. 07-1139 referencing the docket number indicated above.

Respectfully submitted,



E. Stewart Mittler
Reg. No. 50,316

October 21, 2008

GERON CORPORATION
230 Constitution Drive
Menlo Park, CA 94025
Telephone: (650) 566-7237
Fax: (650) 473-8654